Data Evaluation Report on the Acute Oral Toxicity of IR5878 (Orthosulfamuron) on Bobwhite quail (*Colinus virginianus*)

EPA MRID Number 46260108

Data Requirement:	PMRA DATA CODE	
	EPA DP Barcode	D304186
	OECD Data Point	
	EPA MRID	46260108
	EPA Guideline	§71-1
	OPPTS Guideline	850.2100

Test material:		IR5878
Purity:		97.99 ± 0.39%
Common name:		Orthosulfamuron
Chemical name:	IUPAC:	Not reported
	CAS name:	Not reported
	CAS No.:	Not reported
	Synonyms:	Not reported

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Staff Scientist, Dynamac Corporation

Signature:
Date: 12/23/04

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Secondary Reviewer: Kristina Garber
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Signature:
Date: 7/27/06

Reference/Submission No.:

Company Code:
Active Code:
EPA PC Code: 108209

Date Evaluation Completed: 31-07-2006

CITATION: Dias, N.A. 2001. IR5878: Acute oral toxicity (LD_{50}) to the Bobwhite quail. Unpublished study performed by Huntingdon Life Sciences, Ltd., Huntingdon, Cambridgeshire, England. Study No. IGA 004/012894. Study sponsored by ISAGRO SpA, Centro Uffici San Siro - Fabbricato D, Milano, Italy. Study initiated March 30, 2001, completed April 13, 2001.

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EXECUTIVE SUMMARY:

The acute oral toxicity of IR5878 (Orthosulfamuron) to 8-month Bobwhite quails (*Colinus virginianus*) was assessed over 14 days. IR5878 (Orthosulfamuron) was suspended in corn oil, and administered to the birds by oral gavage at concentrations of 0 (vehicle control), 500, 1000, and 2000 mg/kg-bw (nominal values, uncorrected for purity). Mean measured does were <0.3 (LOD, control), 500, 988, and 1960 mg a.i./kg-bw.

No mortality was observed in the control or treatment groups. The acute LD_{50} was >1960 mg a.i./kg-bw, the highest level tested. IR5878 (Orthosulfamuron) was categorized as practically non-toxic to Bobwhite quail on an acute oral basis. No clinical signs of toxicity were observed during the study, and no treatment-related effects were observed on feed consumption, body weight change, or upon gross necropsy of the control and high-dose birds at study termination. As a result, the NOEL was 1960 mg a.i./kg-bw.

This toxicity study is scientifically sound and fulfills the guideline requirements for an acute toxicity study using the Bobwhite quail (§71-1). This study is classified as ACCEPTABLE.

Results Synopsis

Test Organism Age: Approximately 8 months old (Young adults)
Test Organism Size: 178-219 g (weight range for all individual birds at test initiation)

LD_{50}: >1960 mg a.i./kg-bw
NOEL: 1960 mg a.i./kg-bw
LOEL: >1960 mg a.i./kg-bw
Endpoint(s) Affected: none

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: The protocol followed procedures of the U.S. EPA Pesticide Assessment Guidelines, FIFRA Subdivision E, Subsection 71-1 (1982). The following deviation from §71-1 was noted:

The pre-test health of the birds (including mortality) during acclimation was not described.

This deviation did not affect the scientific validity or acceptability of this study.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. This study was conducted in accordance with GLP standards set forth by the UK (1999), EC Commission (1999) and OECD (1997).

A. MATERIALS:

1. Test Material IR5878 (Orthosulfamuron)

Description: Powder

Lot No./Batch No.: FCF/T/172-00 (ex 20525/03/8)

Purity: 97.99 ± 0.39%

Stability of Compound Under Test Conditions: N/A

Storage conditions of test chemicals: Room temperature

2. **Test organism**:

Species: Bobwhite quail (*C. virginianus*)

Age at study initiation: Young adult birds, 8 months old

Weight at study initiation: 178-219 g (weight range for all individual birds at test initiation)

Source: Monkfield Nutrition, Church Farm Barn, Hertfordshire, England.

B. STUDY DESIGN:

1. Experimental Conditions

a. Range-finding Study: An initial range-finding study was conducted with Orthosulfamuron at 2000 mg/kg-bw (limit dose) using two adult Bobwhite quail (one per sex). No mortality was observed after 14 days.

b. Definitive Study: See Table 1

Table 1. Experimental Parameters.

Parameter	Details	Remarks
Acclimation period: Conditions (same as test or not): Feeding: Health (any mortality observed):	15 days Same as test Water and Standard HRC pelleted layer diet were provided, *ad libitum*. The pre-test health of the birds (including mortality) during acclimation was not described.	Diet composition was provided on p. 14. No antibiotic was used in the diet (p. 13).
Pen size and construction materials	Pens (0.31 x 0.39 x 0.24 m) were constructed of plastic coated steel wire mesh.	According to the guideline, pens must conform to good husbandry practices and should not create crowding stress.
Test duration	14 Days	-

Parameter	Details	Remarks
Dose preparation	The test substance was administered as a suspension in corn oil.	-
Mode of dose administration	Oral gavage	-
Dose levels nominal: measured:	0 (vehicle control), 500, 1000, and 2000 mg/kg bw <0.03 (<LOD, vehicle control), 50.0, 98.8, and 196.0 mg a.i./mL representing a procedural recovery range of 97.0-99.0.	The nominal dosages were not adjusted for the purity of the test substance (p. 14). Results of test formulation analysis were presented in Table 2, p. 35. Since the amount of each dose was 10 mL/kg-bw, the dose levels for the birds were <0.3, 500, 988 and 1960 mg a.i./kg-bw (reviewer adjusted).
Solvent/vehicle type: amount/bw:	Corn oil 10 mL/kg-bw	The stock solutions were administered at a constant dosing volume of 10 mL/kg-bw (p. 14).
Number of birds per groups/treatment	Control: 10 Treatments: 10	5 males and 5 females per treatment group. 2 or 3 birds per sex for the same treatment group were placed in a cage.
No. of feed withholding days before dosing	Overnight (approximately 19 hours)	-
Test conditions Temperature: Relative humidity: Photo-period:	Minimum: 24°C (mean) Maximum: 26°C (mean) 35% 10-hours light/14-hours dark.	-
Reference chemical, if used	None used	-

2. Observations: See Table 2.

Table 2: Observations.

Parameter	Details
Parameters measured	Mortality Clinical signs of toxicity Individual body weight Average feed consumption Necropsy
Indicate if the test material was regurgitated	None reported
Groups on which necropsies were performed	Gross necropsies conducted on all surviving control and high-dose birds at study termination.
Observation intervals	Mortality and signs of toxicity were observed daily. Body weights were determined on Days 0 (prior to dosing), 7, and 14. Feed consumption was determined weekly.
Were raw data included?	Yes, data for individual bodyweights were provided for days 0, 7 and 14. Data were also provided for weights taken before the test was initiated.

II. RESULTS AND DISCUSSION:

A. MORTALITY:

No mortality was observed in the control or treatment groups. The 14-day LD_{50} was >2000 mg/kg-bw (nominal), the highest concentration tested. The reviewer-calculated 14-day LD_{50} value was > 1960 mg a.i./kg-bw.

B. SUB-LETHAL TOXICITY ENDPOINTS:

No clinical signs of toxicity were observed in the control or any test group during the study. Mean body weight changes and food consumption for males and females, per test group were reported (Tables 3 and 4). No gross abnormalities were detected upon necropsy of the control and high-dose birds at study termination. No treatment related effects on body weight changes or food consumption were observed. Statistical analyses were not conducted on sub-lethal endpoints. Based on the assumption that there were no significant differences in body weight and food consumption of control groups and test groups, the NOEC was 1960 mg a.i./kg-bw (reported as 2000 mg/kg-bw) and the LOEC was >1960 mg a.i./kg-bw.

Table 3: Mean body weight changes (in g) of male and female bobwhite quail (*Colinus virginianus*) during testing.

Treatment Dose, mg a.i./kg-bw Measured (Nominal, mg/kg-bw)	Males		Females	
	Days 0-7	Days 7-14	Day 0-7	Day 7-14
Vehicle control	+3	-1	+5	-2
500 (500)	+4	0	+5	+2
988 (1000)	+5	0	+4	0
1960 (2000)	+3	0	+5	0
NOEL	1960 mg a.i./kg-bw		1960 mg a.i./kg-bw	
LOEC	>1960 mg a.i./kg-bw		>1960 mg a.i./kg-bw	

Table 4: Mean daily feed consumption (g/bird/day) of male and female bobwhite quail (*Colinus virginianus*) during testing.

Treatment Dose, mg a.i./kg-bw Measured (Nominal, mg/kg-bw)	Males		Females	
	Days 1-7	Days 8-14	Days 1-7	Days 8-14
Vehicle control	10	10	11	10
500 (500)	11	11	11	11
988 (1000)	11	11	12	12
1960 (2000)	11	12	12	12
NOEL	1960 mg a.i./kg-bw		1960 mg a.i./kg-bw	
LOEC	>1960 mg a.i./kg-bw		>1960 mg a.i./kg-bw	

C. REPORTED STATISTICS:

The reported results were based on nominal concentrations, which were uncorrected for test substance purity. Since there were no mortalities observed in this study, the LD_{50} value was assumed to be greater than the highest concentration tested. Neither body weight nor feed consumption data were statistically compared. Based on the assumption that there were no significant differences in body weight and food consumption of control groups and test groups, the NOEC was reported to be the highest nominal concentration tested (2000 mg/kg-bw).

D. VERIFICATION OF STATISTICAL RESULTS:

The study report identified the units of measured concentrations as "mg/mL." The reviewer assumed that this was equivalent to mg a.i./mL IR5878 (Orthosulfamuron). The reviewer converted the nominal treatment

concentrations and resulting nominal toxicity values to measured values using the reported measured concentrations, multiplied by the volume of test substance administered per kg-bw to achieve values in mg a.i./kg-bw. Since there were no mortalities observed in this study, the LD_{50} value was assumed to be greater than the highest concentration tested (1960 mg a.i./kg-bw.).

Neither body weight nor feed consumption data were statistically compared in the report. A qualitative review of the data did not reveal any obvious concerns of significant differences in changes in mean body weights or food consumption (Tables 3 and 4). Based on the assumption that there were no significant differences in body weight and food consumption of control groups and test groups, the NOEC was assumed to be the highest concentration tested.

E. STUDY DEFICIENCIES:

There were no significant deviations from U.S. EPA Guideline §71-1 that affected the validity or acceptability of this study.

F. REVIEWER'S COMMENTS:

The reviewer's conclusions were consistent with those of the study authors, except for the basis of the study authors' toxicity values on the nominal concentrations, while the reviewer based them on the measured concentrations.

The toxicity category, "practically non-toxic" is defined by a LD_{50} >2000 mg/kg-bw. Since the LD_{50} for this test was defined as >1960 mg a.i./kg-bw, there is some uncertainty regarding the suitability of this classification. However, since no sublethal effects were observed at 1960 mg a.i./kg-bw, it seems reasonable that an increase in the concentration of the test substance by 2% is unlikely to result in effects resulting in mortality of 50% of tested birds.

OECD requires water solubility, stability in water and light, pK_a, P_{ow}, and vapor pressure of the test compound. These OECD requirements were not reported.

G. CONCLUSIONS:

This toxicity study is scientifically sound and fulfills the guideline requirements for an acute toxicity study using the Bobwhite quail (§71-1), and is classified ACCEPTABLE. No treatment-related effects on mortality were observed. No clinical signs of toxicity were observed. Qualitative observations of mean data for treatment groups indicated that body weight and food consumption were not affected during the study. The 14-day acute oral LD_{50} was >1960 mg a.i./kg-bw, the highest level tested. The NOEC was the highest treatment level tested. IR5878 (Orthosulfamuron) was classified as practically non-toxic to the Bobwhite quail.

III. REFERENCES:

A reference list was not provided.